CRFC-046

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Ceriani, R.L., et al. : Art Unit 1805
Serial No.: To be Assigned : Examiner -
Filed: Herewith : Schmickel, D.

FOR: FUSION PROTEIN WITH 46 KDALTON HMFG DIFFERENTIATION ANTIGEN BINDING SPECIFICITY, COMPOSITION, KIT & METHODS

INFORMATION DISCLOSURE STATEMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

S I R :

Pursuant to 37 C.F.R. §§ 1.97 and 1.98 and to the duty of disclosure set forth in 37 C.F.R. § 1.56, the Examiner in charge of the above-identified application is requested to consider and make of record the references listed on the PTO 1449 (R&P) submitted herewith.

Under 37 C.F.R. § 1.98(d), copies of the patents and publications listed on the enclosed Form PTO-1449 are not required to be provided, because they were cited by or submitted to the Patent and Trademark Office in prior application, Serial No. 08/607,538, filed November 1, 1990, which is relied upon for an earlier filing date under 35 U.S.C. § 120.

Although the information submitted herewith may be "material" to the Examiner's consideration of the subject application, this submission is not intended to constitute an admission that such information is "prior art" as to the claimed invention.

In accordance with 37 C.F.R. § 1.97(g), the filing of this Information Disclosure Statement shall not be construed to mean that a search has been made.

No fee or certification is required. 37 C.F.R. § 1.97(b).

REMARKS

Applicants wish to provide the following comments on the cited references.

Stubbs et al (1990) disclose the cloning of a 2.1-kilobase cDNA that codes for a surface protein of mammary epithelial cells isolated from a mouse library. This sequence shows a certain degree of identity with C-terminal domains of human coagulation factors VIII and V. These similarities are the basis for predicting possible functions of the protein and its means of interaction with the surface of the cell.

Ceriani et al (1987) disclose the treatment of human breast carcinomas implanted in nude mice with monoclonal antibodies raised against human milk fat globule components. The tumors were treated for a prolonged time with the monoclonal antibody cocktail. This treatment showed, in general, to reduce the size or inhibit the tumors. Those tumors that survived and continued to grow may have little or no antibody specific antigen content.

Ceriani et al (1983) disclose the preparation of hybridomas that secrete monoclonal antibodies against three different surface antigens of normal human mammary epithelial cells. The hybridomas are prepared by fusion of mouse myeloma cells with spleen cells from mice and rats immunized with delipidated human milk fat globules. Three different monoclonal antibodies are said to identify molecules with apparent molecular weights of 46,000, 70,000 and 400,000. The latter is a mucin-like glycoprotein with a high sugar content not previously described as a component of human milk fat globule or of human mammary epithelial cell membranes.

Ceriani and Rosenbaum in Immunodiagnosis of Cancer (1991) is a review describing the use of new immunoassys for circulating antigens that have a direct relationship to breast cancer disease.

Ceriani and Blank (1988) disclose a treatment of human breast tumors with radiolabeled I-131 monoclonal antibodies raised against human milk fat globule. These are some of the antibodies used in the experimental section of this application, e.g., Mc1, Mc3, Mc5 and Mc8. Tumor destruction was shown to be dose dependent. It is shown that the systemic injection of radioiodinated monoclonal antibodies against human milk fat globule destroys epithelial cells of human breast tumors and controls the growth of the tumor for an appreciable length of time. Radiolabeled monoclonal antibodies proved to be more effective than unlabeled monoclonal antibodies in reducing breast tumor mass and also in inhibiting growth for longer periods of time at similar doses.

Peterson et al (1990) disclose the biochemical and histological characterization of antigens preferentially expressed on the surface and cytoplasm of breast carcinoma cells identified by monoclonal antibodies against the human milk fat globule. The monoclonal antibodies Mc8 and Mc3 that bind specifically the 46,000 dalton component stained histologically only malignant breast tissue but only weakly. They bound strongly to intact breast carcinoma cells and breast cell membrane preparations in a radioimmunoassay.

The Ceriani et al (1982) reference relates to the determination of human mammary epithelial antigens (HME-Ags) in sera of patients with disseminated cancer of the breast and other organs. This antigen is

found in high levels in breast cancer patients. Patients with disseminated non-breast cancer as well as normal female controls do not have these high levels. Heterologous, specific antisera against these antigens present in the human milk fat globule membrane and breast epithelial cells were used in a solid-phase radioimmunoassay to determine the presence of the antigens in the sera of patients.

Salinas et al (1987) disclose the use of monoclonal antibodies utilized in this invention, Mc3 and Mc8, prepared against human mammary-epithelial antigens of human milk fat globule membranes to characterize breast carcinoma associated antigens (BCAA), antibodies and circulating immune complexes (CIC).

The Ceriani et al (1977) reference relates to surface differentiation antigens of human mammary epithelial cells carried on the human milk fat globule. In this study, rabbit antibodies against components of the human milk fat globule were shown to bind specifically to normal human breast epithelial cells and cell lines derived from breast carcinomas as well as to the outer surface of the human milk fat globule. Cells derived from other epithelial and ectodermal tissues, fetal fibroblasts, cells of the blood buffy coat and even fibroblasts of the breast itself do not bind the antibodies. This suggests that the antibodies are detecting cell-type specific antigens.

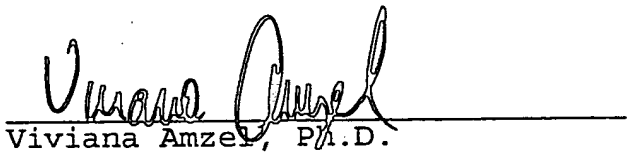
Sasaki et al (1981) provide a quantitation of human mammary epithelial antigens in cells cultured from normal and cancerous breast tissues. This article provides a sensitive radioimmunoassay developed to quantitate the level of human breast cell-type specific antigens on cells

from normal breast and from various established cell lines of breast and non-breast origin. Major proteinaceous components in human milk fat globule membranes were shown to have molecular weights of 150,000, 75,000, 60,000 and 48,000 daltons.

Applicants believe the claimed invention to be patentably distinguishable over the art cited herein.

In view of the foregoing remarks, it is believed that this application is now in condition for examination on the merits and for allowance. Early notice to that effect is hereby solicited.

Respectfully Submitted,



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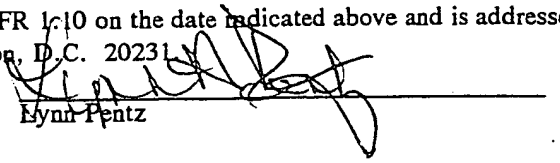

Lynn Pentz

The Commissioner is hereby authorized to charge payment to Deposit Account No. 18-0350 of any fees associated with this communication.

OMB No. 0651-0011 (12/31/88)

INFORMATION DISCLOSURE CITATION

(Use several sheets if necessary)

ATTY. DOCKET NO.	SERIAL NO.
CRFC-046	To be assigned
APPLICANT: R. L. Ceriani et al.	
FILING DATE: Herewith	GROUP

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO

OTHER DOCUMENTS *(Including Author, Title, Date, Pertinent Pages, Etc.)*

		A	Stubbs, J.D., et al, "cDNA cloning of a mouse mammary epithelial cell surface protein reveals the existence of epidermal growth factor-like domains linked to factor VIII-like sequences"
			P.N.A.S. (USA) 87:8417-8421 (1990)
		B	Ceriani, R.L., et al, "Experimental Immunotherapy of Human Breast Carcinomas Implanted in Nude Mice with a Mixture of MOnoclonal Antibodies against Human Milk Fat Globule Components"
			Cancer Research 47:532-540 (1987)

EXAMINER	DATE CONSIDERED

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

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OTHER DOCUMENTS *(Including Author, Title, Date, Pertinent Pages, Etc.)*

		C	Ceriani, R.L., et al, "Characterization of Cell Surface Antigens of Human Mammary Epithelial Cells with Monoclonal Antibodies Prepared Against Human Milk Fat Globule, S.C.G. Vol 9, No.4:415-427 (198
		D	Ceriani, R.L., et al, "Breast Epithelial Antigens in the Circulsation of Breast Cancer Patients", Sec.Ed:223-241 (1991)
		E	Ceriani, R.L., et al, "Experimental Therapy of Human Breast Tumors with ^{131}I-labeled Monoclonal Antibodies Prepared against the Human Milk Fat Blobule", Cancer Research 48:4664-4672 (1988)
		F	Peterson, J.A., et al, "Bi chemical and Hist logical Characterization of Antigens Preferentially Expressed on the Surface and Cytoplasm of Breast Carcinoma Cells Identified by Monoclonal Antibodie Against the Human Milk Fat Globule", HYBRIDOMA Vol 9, No.3: (1990)

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		H	Ceriani, R.L., et al, "Circulating human mammary epithelial antigens in breat cancer", P.N.A.S. (USA) 79:5420-5424 (1982)
		I	Salinas, F.A., et al, "Significance of Breast Carcinoma-associated Antigens as a Monitor of Tumor Burden: Characterization by Monoclonal Antibodies", Cancer Research 47:907-913 (1987)
		J	Ceriani, R.L., et al, "Surface differentiation antigens of human mammary epithelial cells carried on the human milk fat globule", P.N.A.S. (USA) Vol 74, No. 2:582-586 (1977)
		K	Sasaki, Masao, et al, "Quantitation of Human Mammary Epithelial Antigens in Cells Cultured from Normal and Cancerous Breast Tissues", InVitro Vol 17, No 2:0150-0158 (1981)

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Information Disclosure Statement by Applicant (Use several sheets if necessary)	APPLICANT R. L. Ceriani	
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U.S. PATENT DOCUMENTS

Exmr Initial		Document Number	Date	Name	Class	Sub Class	Filing Date
		4,857,635	8/89	Zimmerman et al.			
		4,348,384	9/89	Horikashi et al.			

FOREIGN PATENT DOCUMENTS

Exmr Initial		Document Number	Date	Country	Class	Sub Class	Translation YES	Translation NO

OTHER DOCUMENTS
(Including Author, Title, Date, Pertinent Pages, Etc.)

		1)	Kane et al., "Cloning of a cDNA coding for human factor V, a blood coagulation factor homologous to factor VIII and ceruloplasmin", Proc. Natl. Acad. Sci. USA, Vol. 83, pp. 6800-6804 (Sept. 1986).
		2)	Nakagawa et al., "Purification of Thyroid Peroxidase by Monoclonal Antibody-Assisted Immunoaffinity Chromatography", Biochemical and Biophysical Research Communications, Vol. 127, No. 1, pp. 8-14, (Feb. 1985)

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